

**IN THE DRAWINGS:**

*not attached*  
Enclosed, please find Figs. 7 and 8, with corrections shown in red. In Fig. 7, a typographical error was made wherein reference was made to examples 96-98 rather than examples 96-100. In Fig. 8, a typographical error was made wherein reference was made to examples 99-100 rather than examples 101-104.

**IN THE CLAIMS:**

**Please amend claims 58, 60-62, 67-75, 86, 93-97, 100, 101, 111, 114, 124, 126, 128, 131, 143, 144, 151, 157, 158, 162, 169 and 172 to read as follows:**

58. A combination of substances in a liquid medium comprising:  
at least one first amphiphatic substance selected from lipids, lipid-like materials and combinations thereof;  
at least one second amphiphatic substance selected from edge-active substances, surfactants and combinations thereof; and  
at least one third amphiphatic substance selected from chain molecules;  
wherein the first substance and the second substance form extended surfaces in contact with the medium,  
wherein the solubility of the second amphiphatic substance in the liquid medium is greater than the solubility of the first amphiphatic substance in the liquid medium,  
wherein the extended surfaces formed by the first substance are greater than the extended surfaces formed by the second substance,  
wherein the extended surfaces formed by the first substance and the second substance combined are more extended than the extended surfaces formed by the first substance alone,  
wherein molecules of the third substance associate with the extended surfaces formed by the first substance and the second substance,  
wherein the presence of said at least one second substance in the combination increases the ability of the molecules of the third substance to associate with the extended surfaces formed by the at least one first substance and the at least one second substance.

60. The combination of claim 58 wherein the extended surfaces formed by the first and second substance carry a net electric charge and wherein the third substance carries a net electric charge, the molecules of the third substance associating with the extended surfaces, and the net charge density of the surfaces and the net charge of the molecules associating with the surfaces having the same sign.

61. The combination of claim 58 wherein the extended surfaces formed by the first and second substance are negatively charged and wherein the third substance is negatively charged.

62. The combination of claim 58 wherein the extended surfaces formed by the first and second substance are positively charged and wherein the third substance is positively charged.

67. The combination of claim 63 wherein the concentration of the second substance is at least 0.1 % of the relative concentration as defined in claim 66.

68. The combination of claim 63 wherein the concentration of the second substance is from 1 to 80 percent of the relative concentration as defined in claim 66.

69. The combination of claim 63 wherein the concentration of the second substance is from 10 to 60 percent of the relative concentration as defined in claim 66.

70. The combination of claim 63 wherein the concentration of the second substance is from 20 to 50 percent of the relative concentration as defined in claim 66.

71. The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 15 nm and 5000 nm.

72. The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 30 nm and 1000 nm.

73. The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 40 nm and 300 nm.

74. The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 50 nm and 150 nm.

75. The combination of claim 66 wherein the surface is supported by a solid.

86. The combination according to claim 58 wherein the first substance is less soluble in the liquid medium, and/or being the surface-building and/or charge carrying amphipatic substance in the system, is a lipid, whereas the second substance is more soluble in the liquid medium, and/or causing increased surface curvature, flexibility or adaptability and/or being the charge carrying substance, is a surfactant.

93. The combination of claim 58 wherein the first extended surfaces forming substance is selected from the group consisting of lipids, lipids from a biological source, corresponding synthetic lipids, and modifications of such lipids.

94. The combination of claim 93 wherein the first extended surfaces forming substance is selected from the group consisting of glycerides, glycerophospholipids, isoprenoidlipids, sphingolipids, steroids, sterines or sterols, sulphur-containing lipids, a carbohydrate-containing lipids and half-protonated fluid fatty acids.

95. The combination according to claim 93 wherein the first extended surfaces forming substance is selected from the group consisting of phosphatidylcholines, phosphatidylethanolamines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids,

phosphatidylserines, sphingomyelins, sphingophospholipids, glycosphingolipids, cerebroside, ceramidpolyhexosides, sulphatides, sphingoplasmalogenes, and gangliosides.

96. The combination according to claim 93 wherein the first extended surfaces forming substance is selected from the group consisting of diacyl-, dialkenoyl- and dialkyl-lipids.

97. The combination according to claim 93 wherein the first extended surfaces-forming substance is selected from the group consisting of dioleoyl-lipids, dilinoleyl- lipids, dilinolenyl- lipids, dilinolenoyl- lipids, diarachidoyl- lipids, dilauroyl- lipids, dimyristoyl- lipids, dipalmitoyl- lipids, distearoyl- lipids, and sphingosine- lipids.

100. The combination of claim 98 wherein the surfactant is selected from the group consisting of nonionic, zwitterionic, anionic and cationic surfactants.

101. The combination of claim 98 wherein the surfactant is selected from the group, consisting of long-chain fatty acids or long-chain fatty alcohols, alkyltrimethyl-ammonium salts, alkyldimethyl-ammonium salts, alkylmethyl-ammonium salts, alkylsulphate salts, monovalent salts of cholate, deoxycholates, glycocholates, glycodeoxycholates, taurodeoxycholates, taurocholates, acyl dimethyl-aminioxides, alkanoyl dimethyl-aminioxides, dodecyl dimethyl-aminoxide, alkyl-N-methylglucamides, alkanoyl-N-methylglucamides, N-alkyl-N,N-dimethylglycines, 3-(acyldimethylammonio)-alkanesulphonates, N-acyl-sulphobetaines, polyethylen-glycol-octylphenyl ethers, nonaethylen-glycol-octylphenyl ether, polyethylene-acyl ethers, nonaethylen-dodecyl ether, polyethyleneglycol-isoacyl ethers, octaethyleneglycol-isotridecyl ether, polyethylene-acyl ethers, octaethylenedodecyl ether, polyethyleneglycol-sorbitane-acyl esters, polyethylenglykol-20-monolaurate (Tween 20), polyethylenglykol-20-sorbitan-monooleate (Tween 80), polyhydroxyethylene-acyl ethers, polyhydroxyethylene-lauryl ethers, polyhydroxyethylene-myristoyl ethers, polyhydroxyethylene-cetylstearyl ethers, polyhydroxyethylene-oleoyl ethers, polyhydroxyethylen-4, or 6, or 8, or 10, or 12-lauryl ethers (Brij series), or in the corresponding esters, polyhydroxyethylen-8-stearate (Myrj 45), polyhydroxyethylen-laurates, polyhydroxyethylen-oleates, polyethoxylated castor oil 40

(Cremophor EL), sorbitane-monoalkylates, sorbitane-monolaurate, acyl-N-methylglucamides, alkanoyl-N-methylglucamides, decanoyl-N-methylglucamide, dodecanoyl-N-methylglucamide, alkyl-sulphates, alkyl sulphate salts lauryl-sulphate, oleoyl-sulphate, sodium deoxycholate, sodium glycodeoxycholate, sodium oleate, sodium taurate, fatty acid salts, sodium elaidate, sodium linoleate, sodium laurate, lysophospholipids, n-octadecylene-glycerophosphatidic acid, octadecylene-phosphorylglycerol, octadecylene-phosphorylserine, n-acyl-glycero-phosphatidic acids, lauryl glycero-phosphatidic acids, oleoyl-glycero-phosphatidic acid, n-acyl-phosphorylglycerol, lauryl-phosphorylglycerol, oleoyl-phosphorylglycerol, n-acyl-phosphorylserine, lauryl-phosphorylserine, oleoyl-phosphorylserine, n-tetradecyl-glycero-phosphatidic acid, n-tetradecyl-phosphorylglycerol, n-tetradecyl-phosphorylserine, corresponding palmitoeloyl-, elaidoyl-, vaccenyl-lysophospholipids, corresponding short-chain phospholipids, and surface-active polypeptides.

105. The combination of claim 58 wherein the surface-supporting at least one first substance is a phosphatidylcholine and/or a phosphatidylglycerol and the at least one second substance less capable of forming the extended surface is a lysophospholipid, a lysophosphatidic acid, methylphosphatidic acid, lysophosphatidylglycerol, lysophosphatidylcholine, a partially N-methylated lysophosphatidylethanolamine, a monovalent salt of cholate, deoxycholate, glycocholate, glycodeoxycholate, or a sufficiently polar sterol derivative, a laurate, myristate, palmitate, oleate, palmitoleate, elaidate or other fatty acid salt and/or a Tween-, a Myrj-, or a Brij-surfactant, or a Triton, a fatty acid sulphonate, -sulphobetaine, -N-glucamide or -sorbitane surfactant.

111. The combination of claim 110 wherein the at least one third substance associating with the extended surface is a chain molecules, selected from the group consisting of oligomers or polymers.

114. The combination of claim 111 wherein the chain molecules have an average molecular weight above 1500 Daltons.

124. The combination of claim 123 wherein the polynucleotides are selected from the group consisting of DNA and RNA, in the natural form or after chemical, biochemical, or genetic modification.

126. The combination of claim 58 wherein the third substance acts as an adrenocorticoid, a  $\beta$ -adrenolyte, an androgen an antiandrogen, an antiparasite, an anabolic, an anaesthetic, an analgesic, an analeptic, an antiallergenic, an antiarrhythmic, an antisclerolytic, an antiasthmatic, a bronchospasmolytic, an antibiotic, an antidrepressant, an antipsychotic, an antidiabetic, an antidote, an antiemetic, an antiepileptic, an antifibrinolytic, an anticonvulsive, an anticholinergic, an enzyme, a coenzyme or corresponding inhibitor, an antihistamine, an antihypertensive agents, a biological inhibitor of drug activity, an antihypotensive, an anticoagulant, an antimycotic, an antimyasthenic, an agent against Parkinson or Alzheimer, an antiphlogistic, an antipyretic, an antirheumatic, an antiseptic, a respiratory [analepticum] analeptic or a respiratory stimulant, a anti-bronchitis agent, a cardiotonic, a chemotherapeutic agent, a coronary dilator, a cytostatic, a diuretic, a ganglion-blocker, a glucocorticoid, an anti-influenza agent , a haemostatic, a hypnotic, an immunoglobulin or its fragment, an immunologically active substance, a bioactive carbohydrate, a bioactive carbohydrate derivative, a contraceptive, an anti-migraine agent, a mineralocorticoid, a morphine-antagonist, a muscle relaxant, a narcotic, a neurotherapeutic, a neuroleptic, a neurotransmitter or its antagonist, a peptide, a peptide derivative, an ophthalmic agents, a sympathomimetic agent or a sympatholytic agent, a para- sympathomimetic agent or a para- sympatholytic agent, a protein, a proteine derivative, a psoriasis drug, a neurodermatitis drug, a mydriatic, a psychostimulant, rhinologicum, a sleep-inducing agent or its antagonist, a sedating agent, a spasmolytic, tuberculostatic , urologic agent, a vasoconstrictor or vasodilator agents, a antiviral, a wound-healing substance, or a combination thereof.

128. The combination of claim 58 wherein the third substance has immunomodulating properties, and is selected from the group consisting of antibodies, cytokines, lymphokines, chemokines and correspondingly active parts of plants, bacteria, viruses, pathogens, immunogens, or parts or modifications thereof.

131. The combination of claim 58 wherein the third substance is a recognition molecule, selected from the group consisting of adherins, antibodies, catenins, selectins, chaperones, or parts thereof.

143. The combination of claim 183 wherein the interferon is selected from the group comprising Interferon alpha, beta and gamma.

144. The combination of claim 183 wherein the composition contains up to 20 relative wt-% interferon.

151. The combination of claim 58 wherein the third substance is immunoglobulin (Ig).

157. A method of preparing a combination according to claim 58 in the form of a formulation of a biologically, cosmetically and/or pharmaceutically active agent, comprising:  
selecting the at least one first and the at least one second substance,  
forming extended surfaces, when the first and second substances are combined in contact with said medium,  
selecting the at least one third substance,  
allowing the molecules of the third substance to associate with the extended surfaces formed by the at least one first and the at least one second substance.

158. The method of claim 173 or 174 wherein the means of controlled mechanical fragmentation are selected from the group comprising filtration, pressure change or mechanical homogenisation, shaking, stirring, and mixing.

161. A method for the preparation of a formulation for non-invasive application of active agents, wherein surfaces capable of associating with the active agent are formed from at least one first substance being an amphiphilic substance, at least one hydrophilic fluid, at least one second substance being an edge active substance or surfactant, and at least one third

substance being said active agent, wherein the method comprises separately mixing the at least one first substance, the at least one second substance, the at least one hydrophilic fluid and the at least one third substance, followed by combining the resulting mixtures to subsequently induce the formation of the surfaces which associate with the active agent.

162. The method of claim 161 wherein the active agent is selected from the group consisting of anti-diabetic agents, growth factors, immunomodulators, enzymes, recognition molecules, adrenocorticoid, and adrenolyte.

169. The method of claim 158 wherein several filters are used sequentially or in parallel.

172. A method for providing a pharmaceutical composition comprising:  
in a combination of claim 58, providing the extended surfaces in the form of membranes formed by the at least one first substance and the at least one second substance surrounding miniature droplets, wherein the at least one third substance being a drug associates with said droplet surface to be carried by said droplets to the place where the drug is intended to act.

**Kindly add the following new claims:**

173. The method of claim 157 further comprising: utilizing controlled mechanical fragmentation to form extended surfaces.

174. The method of claim 157 further comprising the step of generating the extended surfaces by means of controlled mechanical fragmentation in the presence of the third substance or before the addition of the third substance, such that the third substance associates with the extended surfaces formed by controlled mechanical fragmentation.

175. The combination of claim 65 wherein the concentration of the second substance is at least 0.1 % of the relative concentration as defined in claim 66.



176. The combination of claim 65 wherein the concentration of the second substance is from 1 to 80 percent of the relative concentration as defined in claim 66.

177. The combination of claim 65 wherein the concentration of the second substance is from 10 to 60 percent of the relative concentration as defined in claim 66.

178. The combination of claim 65 wherein the concentration of the second substance is from 20 to 50 percent of the relative concentration as defined in claim 66.

179. The combination of claim 66 wherein the concentration of the second substance is at least 0.1 % of the relative concentration as defined in claim 66.

180. The combination of claim 66 wherein the concentration of the second substance is from 1 to 80 percent of the relative concentration as defined in claim 66.

181. The combination of claim 66 wherein the concentration of the second substance is from 10 to 60 percent of the relative concentration as defined in claim 66.

182. The combination of claim 66 wherein the concentration of the second substance is from 20 to 50 percent of the relative concentration as defined in claim 66.

183. The combination of claim 1, wherein said at least one third substance is interferon being suitable for use in humans or animals.

184. The combination of claim 183, wherein interferon is included in an amount ranging from about 0.1 to about 15 mg interferon/mL.

185. The combination of claim 183, wherein interferon is included in an amount ranging from about 1 to about 10 mg interferon/mL.

186. The use of the combination of claim 58 for medicinal or biological applications.
187. The use of the combination of claim 58 for the preparation of drug carriers or drug depots.
188. The use of the combination of claim 58 for bioengineering or for genetic manipulations.
189. The use of the combination of claim 58 for separation technology, (bio)processing or diagnostic purposes.
190. The use of the combination of claim 58 to stabilize surface-associating molecules and/or in catalysing processes which involve molecules in the surface-associated state.
191. The use of the combination of claim 190 for chain molecules that are at least partially amphipathic.
192. The use of the combination of claim 191, wherein the chain molecules are proteins, polypeptides, polynucleotides or polysaccharides.
193. The use of the combination of claim 58 to affect the kinetics and/or the reversibility of association or dissociation between surface-associating molecules and a complex, adaptable surface.

#### **REMARKS**

Claims 58-172 are pending in the subject application. Claims 58, 60-62, 67-75, 86, 93-97, 100, 101, 111, 114, 124, 126, 128, 131, 143, 144, 151, 157, 158, 162, 169 and 172 have been amended for clarification purposes. Claims 173-193 have been added. Support for the amendment to claims 58, 60-62, 67-75, 86, 93-97, 100, 101, 111, 114, 124, 126, 128, 131, 143,